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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/040,945	01/09/2002	Randy R. Robinson	0610.00500OI/MAC	5282

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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 06/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/040,945	ROBINSON ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/24/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 7-15 and 17-94 have been canceled.

Claims 4 and 16 have been amended.

2. Claims 1-6 and 16 are pending and under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. This Office Action contains a New Ground of Objection.

5. It is noted that Applicant's response filed 5/24/2005 states that the response is filed in reply to the final office action mailed November 24, 2004, however, the office action mailed November 24, 2004 was a non-final office action, not a final office action. This Office Action is the final Office Action.

Objections/Rejections Withdrawn

6. The objection of claim 16 as depending from claims drawn to a non-elected invention is withdrawn in view of the amendment to the claim.

7. The rejection of claim 16 under 35 U.S.C 101 as being drawn to non-statutory subject matter is withdrawn in view of the amendment to the claim.

8. The rejection of claims 4-6 under 35 U.S.C. 112, second paragraph, as being indefinite for lack of antecedent basis in the claims is withdrawn in view of the amendments to the claim 4.

9. The rejection of claim 16 under 35 U.S.C. 112, second paragraph, as being indefinite for reciting "linked" is withdrawn in view of applicant's arguments and upon further consideration.

10. The rejection of claims 1-6 and 16 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, and 4 of U.S, Patent 5,595,898 is withdrawn in view of the terminal disclaimer filed 5/24/2005, and now accepted.

11. The rejection of claim 16 under 35 U.S.C. 102(b) as being anticipated by Skerra et al (Science 240:1038-1041, May 1988, Ids reference AR45) is withdrawn in view of applicants arguments and the submission of copies of priority applications 07/077,528 and 07/142,039 providing adequate written support for claim 16 as of 7/24/1987.

12. The rejection of claim 16 under 35 U.S.C. 102(b) as being anticipated by Better et al (Science 240:1041-1043, May 1988, Ids reference AR5) is withdrawn in view of applicants arguments and the submission of copies of priority applications 07/077,528 and 07/142,039 providing adequate written support for claim 16 as of 7/24/1987.

Response to Arguments

13. The rejection of claim 2 under 35 U.S.C. 112, second paragraph, as being indefinite for reciting "chimeric" is maintained.

The response filed 5/24/2005 has been carefully considered, but is deemed not to be persuasive. The response states the skilled artisan would be reasonable apprised of then metes and bounds of the claim as written based on the explanation of "chimeric immunoglobulin" that is in the specification, for example at page 48. In response to this argument, the specification discloses a chimeric immunoglobulin, however, the claims are drawn to chimeric heavy and light chains and the metes and bounds of the term "chimeric" or the defining structural features of the chimeric heavy and light chains are unclear. Are the heavy and light chains chimeric as in a humanized antibody wherein non-human CDRs are inserted into human framework regions or is the antibody/immunoglobulin chimeric such that it contains non-human variable regions fused to human constant regions or are the heavy and light chains fused to some non-immunoglobulin molecule such that they are chimeric? One of skill in the art would not be reasonably apprised of the metes and bounds of the claimed chimeric heavy and light chains.

14. The rejection of claims 1-6 under 35 U.S.C. 112, first paragraph because the specification, while being enabling for a polynucleotide molecule encoding an immunoglobulin/antibody or antigen-binding fragment thereof, said polynucleotide molecule comprising a promoter region in operable linkage to a dicistronic transcription unit, said unit encoding a heavy chain and a light chain, wherein the

immunoglobulin/antibody binds antigen, does not reasonable provide enablement for all of the embodiments encompassed by the claims is maintained.

The response filed 5/24/2005 has been carefully considered, but is deemed not to be persuasive. The response states that the claims are enabled as written and that the enablement standard does not require claims recite that the encoded antibody bind antigen. In response to this argument, the claims are drawn to a nucleic acid encoding a heavy chain immunoglobulin and fragments thereof and a light chain immunoglobulin, which are incomplete antibodies that do not contain complete heavy chain and light chain variable regions. Thus, the claims encompass molecules comprising a fragment of a heavy chain and a light chain. As stated in the previous Office Action, it is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Consistent with this, the teachings in applicant's specification are limited to polynucleotides encoding antibodies or immunoglobulins comprising both a heavy chain

and a light chain and the antibody/immunoglobulin binds antigen. The specification does not teach antibodies/immunoglobulins comprising a fragment of the heavy chain immunoglobulin and a light chain immunoglobulin that bind antigen as claimed. Further, it is unclear what is meant by a heavy chain immunoglobulin and a light chain immunoglobulin since the heavy and light chains are only part of an immunoglobulin as evidenced by Exhibit E "Summary of Opinions to be Offered by DR. Gregg Silverman" (IDS filed 5/24/2005), which states "Immunoglobulin" means a full-length, fully folded and assembled polypeptide molecule consisting of two light chain polypeptides and two heavy chain polypeptides (H_2L_2)...". Rudikoff et al cited by the examiner evinces the unpredictability in the art that even minor changes in the in the amino acid sequences of the heavy and light chain variable regions, particularly the CDRs, may dramatically effect antigen-binding function. Thus, it is unlikely that antibodies/immunglobulins comprising only a fragment of the heavy chain and a light chain as defined by the claims have antigen-binding function and the claims do not contain any functional language (i.e., "binds antigen"). Further, a fragment of the heavy chain can be any one of the constant regions, any one of the CDRs, any one of the frameworks, the hinge region or even a single amino acid, which when paired with the light chain would not bind antigen. Thus, one skilled in the art would not know how to use the encompassed molecules, which do not bind antigen as broadly defined by the claims. Applicant has not provided any evidence that the broadly encompassed molecules, which are incomplete antibodies bind antigen with any predictability or reasonable expectation of success.

For these reasons the rejection is maintained.

15. The rejection of claim 16 under 35 U.S.C. 102(b) as being anticipated by either of Wood et al, Sharon et al, Ochi et al, Morrison et al, Cabilly et al, or Boulianne et al is maintained.

The response filed 5/24/2005 has been carefully considered, but is deemed not to be persuasive. With respect to each of the above cited anticipatory references, applicant argues that each reference does not describe a polynucleotide molecule according to claim 16. In response to this argument, applicant has not pointed to anything in the claim that distinguishes the claimed polynucleotide comprising a heavy chain immunoglobulin molecule linked to a polypeptide secretion signal or a light chain immunoglobulin molecule linked to a polypeptide secretion signal over the heavy and light chain immunoglobulin molecules linked to a polypeptide secretion signal of the prior art. Therefore, the rejection is maintained for reasons of record.

16. The rejection of claim 16 under 35 U.S.C. 102(b) as being anticipated by Early et al (Cell. 19:981-992, 1980) is maintained.

The response filed 5/24/2005 has been carefully considered, but is deemed not to be persuasive. The response states argues that Early et al does not describe a polynucleotide molecule according to claim 16. In response to this argument, applicant has not pointed to anything in the claim that distinguishes the claimed polynucleotide

comprising a heavy chain immunoglobulin molecule linked to a polypeptide secretion signal over the heavy chain immunoglobulin molecule linked to a polypeptide secretion signal taught by Early et al (see Fig. 3 and page 984). At page 984, right column Early teaches that immunoglobulin polypeptides are translated with a hydrophobic amino terminal "signal peptide" and such peptides appear to play a role in protein secretion. Therefore, the rejection is maintained.

17. The rejection of claim 16 under 35 U.S.C. 102(b) as being anticipated by Zemel-Dreason et al (Gene. 27(3):315-322, 1984, Ids reference AR53) is maintained.

The response filed 5/24/2005 has been carefully considered, but is deemed not to be persuasive. The response states argues that Zemel-Dreason et al does not describe a polynucleotide molecule according to claim 16.. In response to this argument, applicant has not pointed to anything in the claim that distinguishes the claimed polynucleotide comprising a light chain immunoglobulin molecule linked to a polypeptide secretion signal over the light chain immunoglobulin molecule linked to a polypeptide secretion signal taught by Zemel-Dreason et al. It is reiterated that Zemel-Dreason et al teach plasmids containing the entire coding sequence of L-321 including the signal peptide (pTI27) and/or the β-lactamase signal peptide (pRI12/B13) (see Figures 3 and 1) and the polypeptides were secreted (see Table 1 and pages 320-321). It is the examiner's position that any immunoglobulin chain, which is secreted from a

host cell must have had, prior to secretion, a secretion signal. Therefore, the rejection is maintained.

18. The rejection of claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Gillies et al (Cell. 33:717-728, 1983, Ids reference AR15) is maintained.

The response filed 5/24/2005 has been carefully considered, but is deemed not to be persuasive. The response states that Gillies et al does not describe a polynucleotide molecule according to claim 16. In response to this argument, applicant has not pointed to anything in the claim that distinguishes the claimed polynucleotide comprising a heavy chain immunoglobulin molecule linked to a polypeptide secretion signal over the heavy chain immunoglobulin molecule linked to a polypeptide secretion signal taught by Gillies et al. It is reiterated that Gillies et al teach the expression of the immunoglobulin heavy chain (see Figure 2) and it is the examiner's position that any immunoglobulin chain, which is secreted from a host cell must have had, prior to secretion, a secretion signal. Therefore, the rejection is maintained.

19. The rejection of claim 16 is rejected under 35 U.S.C. 102(e) as being anticipated by Cabilly et al (U.S. patent 4,816,567, filed 4/8/1983, Ids reference P05) is maintained.

The response filed 5/24/2005 has been carefully considered, but is deemed not to be persuasive. The response states argues that Cabilly et al does not describe a polynucleotide molecule according to claim 16. In response to this argument, applicant

has not pointed to anything in the claim that distinguishes the claimed polynucleotide comprising a heavy chain immunoglobulin molecule linked to a polypeptide secretion signal or a light chain immunoglobulin molecule linked to a polypeptide secretion signal over the heavy chain immunoglobulin molecule linked to a polypeptide secretion signal and the light chain immunoglobulin molecule linked to a polypeptide secretion signal of Cabilly et al (see column 13, lines 5-18). Therefore, the rejection is maintained

New Ground of Objection

20. The disclosure is objected to because of the following informalities:

The amendment to the specification filed 5/24/2005 cancelled the benefit claim to PCT/US86/02269 and USSN 06/793,980, however, these cases remain fully incorporated by reference (see last 2 lines of the first paragraph of page 1 titled "CROSS REFERENCE TO RELATED APPLICATIONS"). Clarification is requested.

Appropriate correction is required.

Conclusions

21. No claim is allowed.

22. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827

LARRY R. HELMS, PH.D
PRIMARY EXAMINER